Animal African Trypanosomosis

Disease Monograph Series – 10

Parasite | Protozoa | *Trypanosoma congolense* | *T. brucei brucei* | *T. vivax*
Cattle | Pigs | Camels | Goats | Sheep

IDRC | Bartay

This monograph forms part of a series of disease monographs commissioned by the International Development Research Centre over the period Nov 2015 to April 2016 to inform funding priorities for the Livestock Vaccine Innovation Fund (LVIF). The LVIF is a seven-and-a-half year, CA$57 million partnership between the Bill & Melinda Gates Foundation, Global Affairs Canada and Canada's International Development Research Centre. It focuses on those animal diseases posing the greatest risk to poor livestock keepers in Sub-Saharan Africa, South and Southeast Asia, targeting transboundary diseases to achieve lasting regional impact.

Table of Contents

Acronyms

AAT	Animal African Trypanosomosis
AT	African Trypanosomosis
AU	African Union
AU-IBAR	African Union Inter-African Bureau for Animal Resources
AU-PATTEC	African Union - Pan African Tsetse and Trypanosomiasis Eradication Campaign
BBRSC	Biotechnology and Biological Sciences Research Council
BMGF	Bill and Melinda Gates Foundation
CVO	Chief Veterinary Officer
DALY	Disability-adjusted life year
DIVA	Differentiate infected from vaccinated animals
DVS	Director Veterinary Services
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
IAEA	International Atomic Energy Agency of the United Nations
IM	Intramuscular
NGO	Non-governmental organization
OIE	World Animal Health Organization
PCR	Polymerase chain reaction

SHF	Small holder farmer
SMP-AH	Standard Methods and Procedures in Animal Health Program
Tc	*Trypanosoma congolense*
Tv	*Trypanosoma vivax*
TPP	Target Product Profile
WHO	World Health Organization of the United Nations

Executive Summary

Etiology and relevance

Tsetse-transmitted Trypanosomosis (as opposed to non-testse transmitted Trypanosomosis, generally caused by *T. vivax* in Latin America, and *Trypanosoma evansi*) is an infectious disease unique to Africa caused by *T. congolense, T. vivax,* or *T. brucei brucei*, or simultaneous infection with one or more of these trypanosomes. The disease affects both people [Human African Trypanosomosis (HAT) or sleeping sickness] and animals [Animal African Trypanosomosis (AAT) or Nagana] and occurs in 37 sub-Saharan countries covering more than 9 million km^2, an area which corresponds approximately to one-third of the Africa's total land area. The infection threatens an estimated 60 million people and about 50 million head of cattle. It can also cause serious losses in pigs, camels, goats, and sheep.

In East Africa, *T. congolense* is considered to be the single most important cause of AAT in cattle, while it is also of major importance in West Africa. Although *T. vivax* is considered to be less pathogenic for cattle than *T. congolense*, it is nevertheless the most important cause of AAT in West African cattle. *T. vivax* readily persists in areas free of tsetse flies (for example, in Central and South America and in the Caribbean), where it is transmitted mechanically by biting flies or contaminated needles, syringes, and surgical instruments.

Several types of *T. congolense* can be distinguished by molecular biology; the most common and pathogenic one in cattle is the type “savannah” (large variation in pathogenicity within the savannah subgroup), the other ones (type “forest” and “Kilifi” or Kenya coast) are less pathogenic and have different host affinity.

Epidemiology

While Cattle, sheep, goats, pigs, horses, camels, dogs, cats, and monkeys are susceptible to AAT and may suffer syndromes ranging from subclinical mild or chronic infection to acute fatal disease, more than 30 species of wild animals can be infected with pathogenic trypanosomes, and many of these remain carriers of the organisms. Ruminants are widely known to be active reservoirs of the trypanosomes. Wild Equidae, lions, leopards, and wild pigs are all susceptible and can also serve as carriers of trypanosomes.

AAT occurs where the tsetse fly vector exists in Africa, between latitude 15°N and 29°S, although due to its ability to be mechanically transmitted, *T. vivax* has spread beyond these limits.

Of the 32 species of tsetse fly, *Glossina spp*; known to be competent to carry the 3 AAT agents, 3 species are the major vectors: *Glossina morsitans*, which favors the open woodland of the savanna, *G. palpalis*, which prefers the shaded habitat immediately adjacent to rivers and lakes; and *G. fusca*, which favors the high, dense forest areas.

Transmission of trypanosomes is essentially cyclical: they are transmitted through the bite of an infected tsetse fly. Tsetse flies get the infection when feeding on an infected animal; after implementation of the parasitic cycle in the fly (15–21 days) it becomes infective and may remain infective for the rest of its life.

Mechanical transmission also occurs with *T. vivax*, while other forms, such as vertical transmission can occur intra-utero and during partum.

A number of cattle breeds in West Africa have developed Trypanotolerance, or the ability to harbour natural trypanosome infections without developing severe disease symptoms. The most known of these breeds is the *Bos taurus* N'Dama, but also other similar West African taurine breeds. There are also trypanotolerant zebu breeds in East Africa.

Clinical signs of AAT are not always clear cut. In cattle the disease is usually chronic – some animals may slowly recover but usually relapse when stressed. The most important clinical sign is non-regenerative anaemia, and the most common reason animals are unable to function normally. When tsetse challenge is high, morbidity is usually also high. All three species of trypanosomes will eventually cause death in their hosts unless treated.

Economic impact

Every year, AAT causes about 3 million deaths in cattle while approximately 35 million doses of trypanocidal drugs are administered. Nagana has a severe impact on agriculture in sub-Saharan Africa. The economic losses in cattle production alone are in the range of US$ 1.0 - 1.2 billion. A ponderated evaluation extrapolated for the total tsetse-infested lands values total losses, in terms of agricultural Gross Domestic Product, at US$ 4.75 billion per year

African animal trypanosomosis (AAT) is a very important disease of domestic livestock in sub-Saharan Africa. According to the Food and Agriculture Organization of the United Nations (FAO), it is probably the only disease which has profoundly affected the settlement and economic development of a major part of a continent.

Diagnostics

Trypanosomiasis is generally suspected when an animal in an endemic area is anaemic and in poor condition. Confirmation depends on the demonstration of the organism in blood or lymph node smears. When parasitemia is low, smears of buffy coat (obtained by microhematocrit centrifugation) can be useful for demonstration of the parasites. Buffy coat samples are also used for haematocrit and could be also used for PCR. Serological methods exist for antibody, ELISA and Indirect fluorescent antibody test, while different antigen ELISAs have also been developed.

Control

The control of trypanosomoses has not much changed over the last hundred years and still relies on (1) the control of the vector, (2) the use of trypanocidal and prophylactic drugs and (3) the use of trypanotolerant livestock. Another important element is the correct diagnosis of the disease. There is still no vaccine or immunisation method to date for AAT.

Integrated control approaches are generally recommended and have been successfully applied in countries like Ethiopia. They should be encouraged and implemented in as many regions as possible.

Several approaches have been applied and are still in application in different affected and endemic regions. These have included aerial and land spray of different types of insecticides targeting the tsetse flies. Sterile male techniques, which rely on the fact that females mate only once in a lifetime, have been promoted and used in a number of regions; but have been difficult to implement on all types of Glossina and are expensive. Other techniques with mixed results include traps and odour-baited targets impregnated with insecticides.

Trypanocides: The main drugs used for AAT are isometamidium chloride (ISM) which has both curative and prophylactic effects and diminazene aceturate (DA) which has only curative properties. These drugs have been in use for more than half a century. Approximatly 35 million doses of trypanocides are administered every year in sub-Saharan Africa, with ISM, ethidium bromide and DA representing 40%, 26% and 33% respectively. Despite their high usage, the pharmaceutical industries have been unwilling to invest in research for developing new products, leaving farmers to rely on the existing drugs. Farmers currently have easy access to these trypanocides and this has resulted in rampant numbers of substandard and counterfeit drugs, misuse and under-dosage of the medications, actions which have been blamed for the emergence of trypanocidal drug resistance. To date, there are 17 countries in which trypanocidal drug resistance has been reported.

No vaccine to AAT has been developed to date nor likely in the near future because of the ability of trypanosomes to rapidly change variable surface glycoproteins (VSG) in their coats to avoid an effective Immune response (antigenic variation). This also leads to establishment of prolonged infections with intermittent parasitaemias. There are estimated to be about 1,000 VSGs, in the trypanosomal coat, which switch genetically as antibodies are produced by the host.

Alternative approaches have been researched by different group for vaccine development. The most extensively studied has been the concept of anti-disease vaccines, which were inspired by the fact that trypanotolerant cattle can harbour natural trypanosome infections without developing severe disease symptoms. It was then hypothesised that some parasite proteins or virulence factors played a role in the disease process and that an immune response to these factors may contribute to the mechanisms underlying trypanotolerance. Despite the evaluation of several of these factors, the most studied being the congopain, no conclusive and convincing vaccine could be developed. To date few other groups have been working on different approaches, including irradiated Trypanosoma.

The future of AAT vaccines and vaccination

While the development of a vaccine for AAT seems far from reach, it is possible to control and sometimes eradicate the disease and the vector as it has been done in some regions. It has been shown that integrated control approaches are always more effective in controlling AAT. Supporting such approaches should be encouraged in order to improve the livelihood of livestock keepers leaving in endemic affected regions of Africa.

Clinical disease overview

Etiology

In sub-Saharan Africa, animal African Trypanosomosis (AAT) is considered one of the major constraints to livestock production and development, and one of the most important animal diseases - with more than 80 million cattle exposed to infective tsetse fly bites (*T. congolense, T. brucei brucei*) or infective tsetse fly and biting fly bites (*T. vivax*) [5]. It is estimated to cause annual losses that run into billions of dollars. AAT currently causes direct annual losses of some US$ 1.5 billion and, overall, has the effect of limiting Africa's agricultural income to some US$ 4.5 billion a year below its potential level [5][11].

There are two groups of Trypanosomosis that are generally recognised: the tse-tse transmitted and the non-tseste transmitted Trypanosomosis. Tsetse-transmitted trypanosomosis is a disease complex caused by several species of protozoan parasites of the genus Trypanosoma, mainly transmitted cyclically by the genus Glossina (tsetse flies), but also transmitted mechanically by several biting flies (tabanids, stomoxes, etc.) [20].

African trypanosomiasis is an infectious disease of humans and animals of similar aetiology and epidemiology. The causative agents of the disease are protozoan parasites of the genus Trypanosoma that live and multiply extracellularly in blood and tissue fluids of their mammalian hosts and are transmitted by the bite of infected tsetse flies (Glossina sp.). [2].

Animal African trypanosomosis (AAT) or nagana disease is caused by *T. congolense*, *T. vivax* and *T. brucei spp*. In wild animals, these parasites cause relatively mild infections while in domestic animals they cause a severe, often fatal disease. Two tsetse-transmitted parasites, *T. brucei gambiense* and *T. brucei rhodesiense*, cause human African trypanosomiasis (HAT)/sleeping sickness, which affects both humans and animals. [5][11]

Trypanosomes are protozoan parasites of the genus Trypanosoma (Figure 1), order Kinetoplastida. The present monograph will focus on AAT, and more specifically *T. congolense* and *T. vivax,* and, to a lesser extend *T. brucei.* Other important Trypanosoma, but not covered in the present study, can be seen in figure 1 below.

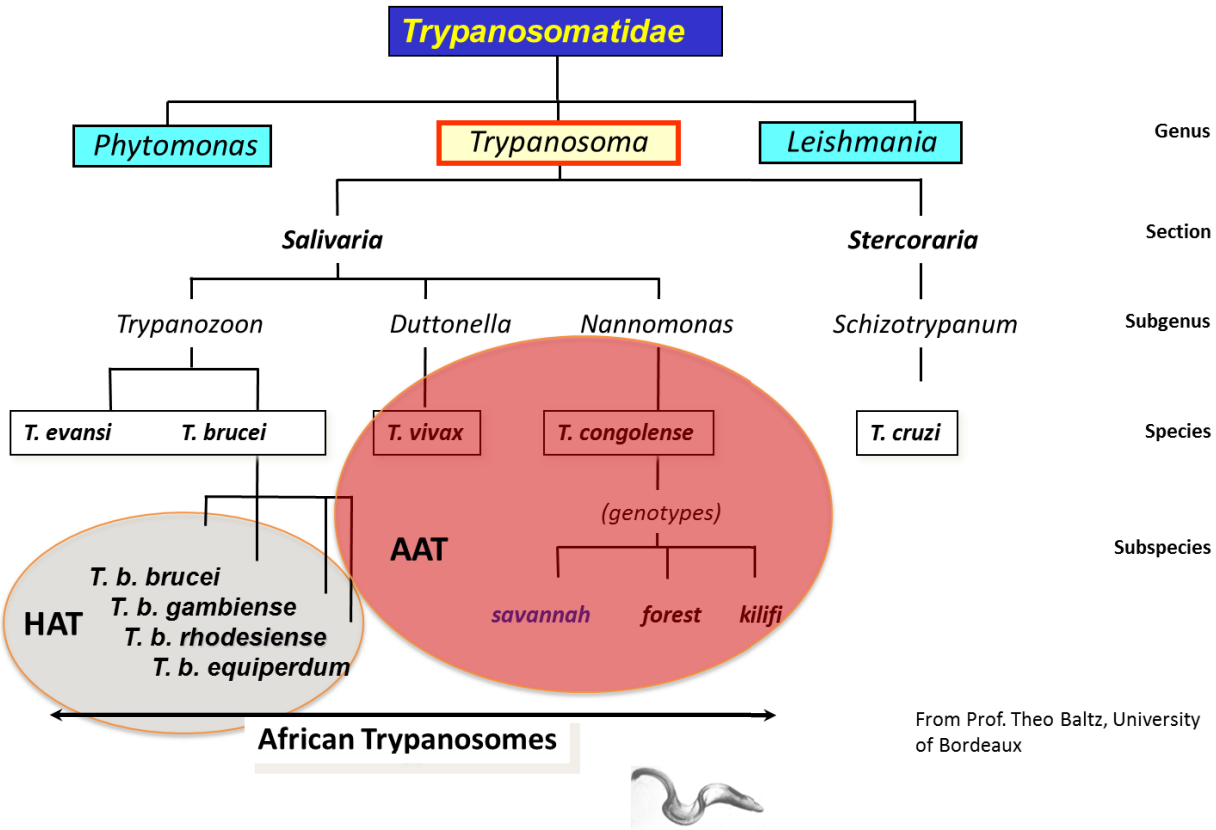


Figure 1: Trypansomatidae classification. Source: Dr Theo Baltz, University of Bordeaux

Trypanosomes have as characteristic organelles, a kinetoplast and a flagellum (Figure 2). Typically, trypanosomes are digenetic parasites and thus require two hosts to complete their life cycle: they multiply in the blood, tissues or body fluids of a vertebrate host (Figure 3). *T. congolense* resides in the subgenus *Nannomonas*, a group of small trypanosomes with medium-sized marginal kinetoplasts, no free flagella, and poorly developed undulating membranes (Figure 2). In East Africa, *T. congolense* is considered to be the single most important cause of AAT. This trypanosome is also a major cause of the disease in cattle in West Africa. [2][11]

T. vivax is a member of the subgenus Duttonella, a group of trypanosomes with large terminal kinetoplasts, distinct free flagella, and inconspicuous undulating membranes. T. vivax is a large (18-26 µm long) monomorphic organism that is very active in wet-mount blood smears. Although this organism is considered to be less pathogenic for cattle than *T. congolense*, it is nevertheless the most important cause of AAT in West African cattle. This trypanosome readily persists in areas free of tsetse flies (for example, in Central and South America and in the Caribbean), where it is transmitted mechanically by biting flies or contaminated needles, syringes, and surgical instruments [2][20].

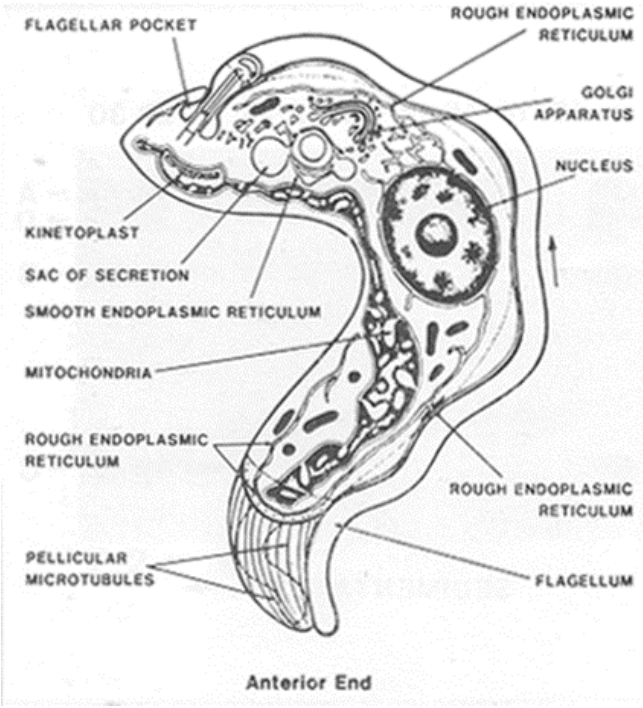


Figure 2: Bloodstream form of T. congolense (source: ILRI info Serv)

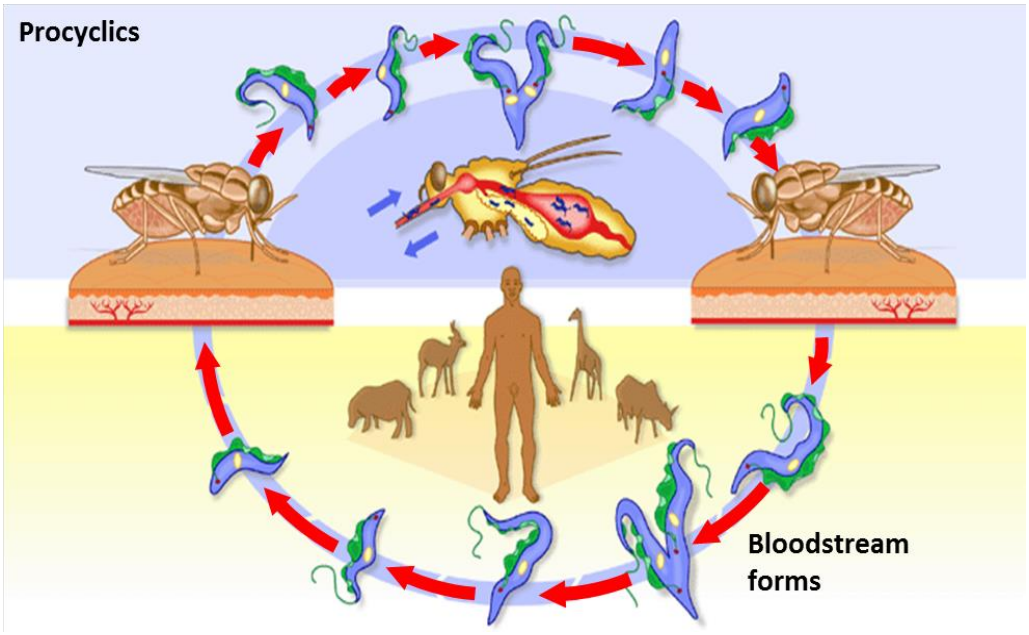


Figure 3: Life cycle of *Trypanosomas* Source: Adama Sow, 2013

Epidemiology

Susceptible animal species

- Cattle, sheep, goats, pigs, horses, camels, dogs, cats, and monkeys are susceptible to AAT and may suffer syndromes ranging from subclinical mild or chronic infection to acute fatal disease. Rats, mice, guinea pigs, and rabbits are useful laboratory species.
- Table 1 below summarises the susceptibility of different domestic mammals and human to different major Trypanosomas.
- More than 30 species of wild animals can be infected with pathogenic trypanosomes, and many of these remain carriers of the organisms. Ruminants are widely known to be active reservoirs of the trypanosomes. Wild equidae, lions, leopards, and wild pigs are all susceptible and can also serve as carriers of trypanosomes.
- *T. vivax* DNA has been found by PCR in crocodiles and monitor lizards in Africa, but whether this organism can become established in reptiles or it is merely inoculated transiently by insect remains to be determined. Experimental infections can be established in laboratory animals including mice, rats, guinea pigs and rabbits [13].
- Certain cattle breed, especially the N'Dama, a *Bos taurus*-type from West Africa, are known to be trypanotolerant, having the ability to survive, reproduce and remain productive under trypanosomosis risk without the aid of trypanocidal drugs [4].

Table 1: Susceptibility of various animal species and humans to different Trypanosomes (Source: adapted by Theo Baltz, University of Bordeaux)

	Cattle	Goats/ sheep	Pigs	Horses/ donkeys	Humans	Location
T congolense	+++ (70% of the problem)	++	+	-	X	Blood (capillary mainly)
T vivax	+++	++	-	++	X	Blood and CNS
T evansi	++	+	++	+++/++ (Surra)	X	
T brucei brucei	+	++	+	+++/++	X	Tissues, blood (low level) and CNS

T brucei gambiense	+	++	+	+++/++	+++ (West A – more chronic)	
T brucei rhodesiense	+	++	+	+++/++	+++ (East A – more acute)	

Distribution

Trypanosomes can be found wherever the tsetse fly vector exists. Tsetse flies are endemic in Africa between latitude 15° N and 29° S, from the southern edge of the Sahara desert to Zimbabwe, Angola and Mozambique. Trypanosomes, particularly *T. vivax,* can spread beyond the "tsetse fly belt" by transmission through mechanical vectors. *T. vivax* is also found in South and Central America and the Caribbean, areas free of the tsetse fly [11].

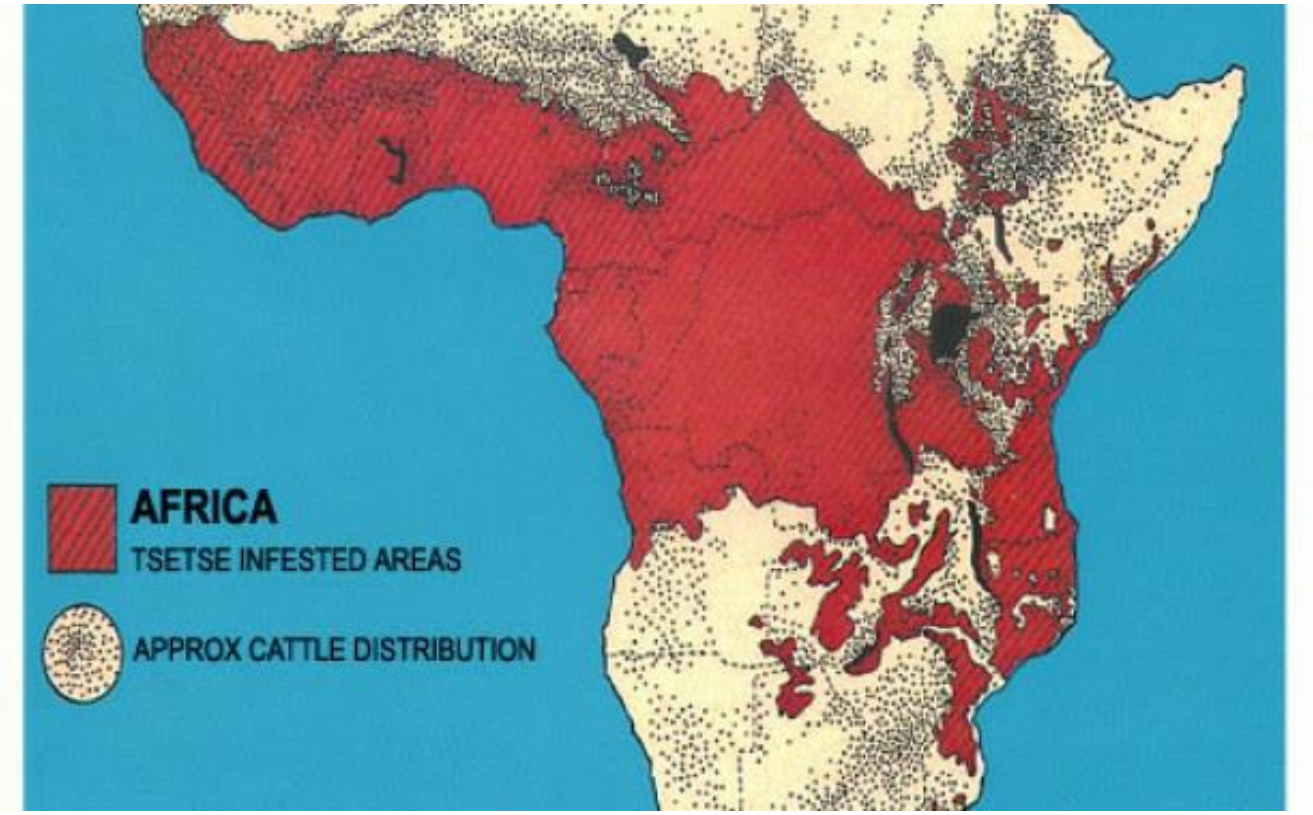


Figure 4: distribution of Tsetse and cattle in Africa (Source PATTEC)

Vectors and Transmission

In Africa, the primary vector for *T. congolense, T. vivax*, and *T. b. brucei* is the tsetse fly. These trypanosomes replicate in the tsetse fly and are transmitted through tsetse fly saliva when the fly feeds on an animal. Although there are up to 23 species of Glossina in sub-Saharan Africa between latitudes 14°N and 29°S that are competent, the three main species of tsetse flies for transmission of trypanosomes are:

- *Glossina morsitans*, which favors the open woodland of the savanna;
- *G. palpalis*, which prefers the shaded habitat immediately adjacent to rivers and lakes; and
- *G. fusca*, which favors the high, dense forest areas. [20]

These tsetse flies remain infected by trypanosomes for life. Trypanosome life cycle involves cyclical development in the tsetse fly, taking up to 3 or more weeks depending on trypanosome species and ambient temperature [2][11]

Trypanosomosis is also mechanically transmitted by tsetse and other biting flies through the transfer of blood from one animal to another. The most important mechanical vectors are flies of the genus Tabanus, but Haematopota, Liperosia, Stomoxys, and Chrysops flies have also been implicated. Mechanical transmission can occur when interrupted feeding is re-started on a new host; thus it is efficient inside a group of animals but has little chance to occur at distance. In Africa, both *T. vivax* and *T. b. brucei* have spread beyond the "tsetse fly belts" [3], where transmission is principally by tabanid and hippoboscid flies.

The vector for *T. vivax* in the Western Hemisphere remains unknown, but several species of hematophagous (especially tabanid and hippoboscid) flies are believed to serve as mechanical vectors.

Figure 5: *Glossina morsitans morsitans* (source Ray Wilson)

Clinical Signs

The course of disease due to infection with trypanosomes is variable and there are no clinical signs specific to bovine trypanosomosis. The manifestations of disease depend upon the degree of damage to specific organs and upon the degree of anaemia. Trypanosomosis in cattle may be acute, subacute or chronic [2]. Furthermore, because simultaneous infections with more than one trypanosome species are very common in most regions, [2], and simultaneous infection with trypanosomes and other hemoparasites (*Babesia spp., Theileria spp., Anaplasma spp.,* and *Ehrlichia spp*.) frequently occurs, it is difficult to conclude which clinical signs are attributable to a given parasite.

The cardinal clinical sign observed in AAT is anemia, which occurs within a week of infection with *T. congolense* and *T. vivax*. There is usually a pronounced decrease in packed cell volume, hemoglobin, red blood cell, and white blood cell levels, and within 2 months these may drop to below 50 percent of their pre-infection values. Also invariably present are intermittent fever, edema and loss of condition. Abortion may be seen, and infertility of males and females may be a sequel. Most cases of trypanosomiasis are chronic, but acute disease, which may be fatal within a week, can also occur.

The severity of the clinical response is dependent on the species and the breed of affected animal and the dose and virulence of the infecting trypanosome. Stress, such as poor nutrition or concurrent disease, plays a prominent role in the disease process [2][5][11].

T. congolense is a hematic trypanosome found only in the blood vessels of the animals it infects. It does not localize and multiply outside blood vessels. Infection with *T. congolense* may result in peracute, acute, or chronic disease in cattle, sheep, goats, horses, and camels. The incubation period is followed by intermittent febrile episodes, depression, lethargy, weakness, loss of condition, anemia, salivation, lacrimation, and nasal discharge. As the disease progresses, loss of condition and hair color changes from black to metallic brown are seen. The back is often arched and the abdomen "tucked up." Anemia is a prominent sign. Early in the infection, the organisms are readily demonstrable in blood smears, but, as the disease progresses to its acute and chronic forms, organisms are most readily demonstrated in lymph node smears. [2][5][11].

T. vivax has a variable incubation period, and, although it is considered to be less virulent for cattle than *T. congolense*, mortality rates of over 50 percent can occur. There seems to be a marked variation in the virulence of different strains of *T. vivax*, but it remains the most important cause of trypanosomosis of cattle, sheep, and goats in West Africa. *T. vivax* is often difficult to find in blood smears and can also be demonstrated in lymph node smears.

The marked immunosuppression resulting from trypanosome infection lowers the host's resistance to other infections and causes in secondary disease, which greatly complicates both the clinical and pathological features of trypanosomiasis [2][8][16]

Diagnosis

Incubation period is generally 8-20 days. *T. congolense* usually becomes apparent in 4–24 days, while *T. vivax* in 4–40 days, and *T. brucei brucei* appearance is highly variable [2][5].

Clinical Diagnosis

Trypanosomiasis should be suspected when an animal in an endemic area is anemic and in poor condition. Confirmation depends on the demonstration of the organism in blood or lymph node smears. Poor nutrition, concurrent diseases, and other stressors often affect the course of AAT, which usually is chronic [2][5][11].

Differential Diagnosis

Acute trypanosomosis with fever should be differentiated with:

- Babesiosis
- Anaplasmosis
- Theileriosis (East Coast Fever)
- Haemorrhagic septicaemia
- Anthrax

Chronic trypanosomosis with anaemia and emaciation:

- Helminthosis
- Malnutrition
- Other haemoparasitoses [11]

Laboratory diagnosis

In the early phases of infection, especially with T. *vivax* and *T. congolense*, the parasite can readily be observed by microscopic examination of a wet-mount of blood slides. Thick blood films and stained with Giemsa are also a good technique (Figure 6). Diagnostic sensitivity is increased significantly by concentrating the parasites prior to examination in combination with a phase-contrast or dark-ground microscope. The centrifugation parasite concentration techniques have the added advantage that the packed cell volume, and hence the level of anaemia, can be determined at the individual animal and/or herd level [20]

Serological methods include antigen and antibody ELISA, and the indirect fluorescent antibody (IFA) test [20]

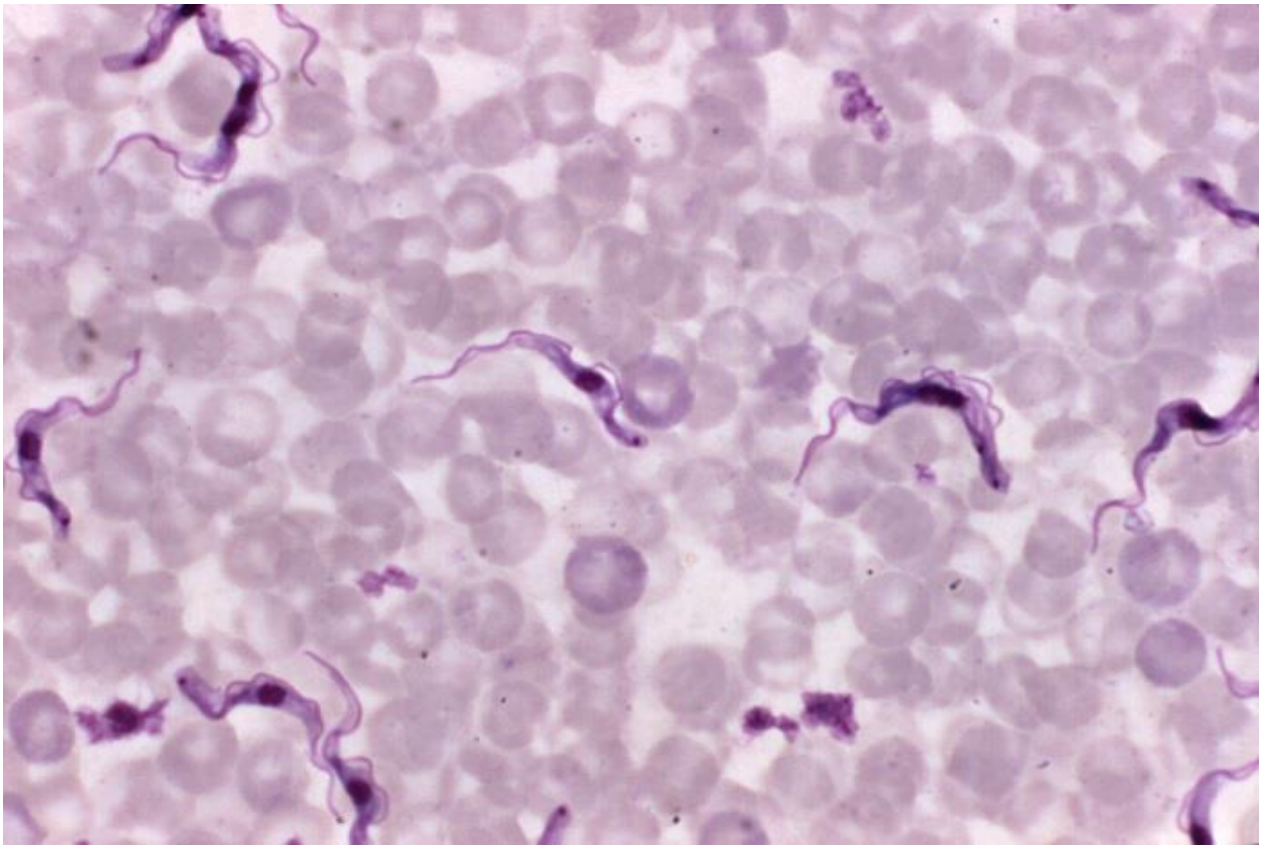


Figure 6: Blood smear with *T. congolense* (source: selenoproteines)

Incidence and Prevalence in Selected Countries

Global

Distribution of AAT has already been described in the previous Section and Figure 4.

Regional

Table 2: Number of AAT outbreaks reported to the OIE between 2005-2015 (Numbers given only for the target countries). Source: OIE.
http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/statusdetail

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
West Africa											
Burkina Faso	+	+	+	+	+	+	+	0	0	+	+
Ivory Coast	3	0	0	+	+	>3	>1	+	+	>5	+
Mali	+	+	?	-	+	-	-	-	-	-	-
Senegal	5	0	+	0	1	0	0	0	0	1	+
East Africa											
Ethiopia	+	+	>4	+	+	+	+	+	+	+	+
Kenya	+	>13	14	?	?	?	?	?	?	9	0
Rwanda	-	?	?	+	+	+	+	9	16	-	-
Tanzania	+	>25	181	49	29	25	22	13	22	27	9

Uganda	+	+	+	+	+	+	+	+	+	+	-
Southern Africa											
Madagascar	0	0	0	0	0	0	0	0	0	0	0
Malawi	+	+	2	+	2	2	0	1	0	-	-
Mozambique	10	5	4	6	3	>4	?	4	2	6	-
South Africa	0	14	15	10	70	5?	+	0	0	0	-
Zambia	-	34	28	61	116	87	+	33	61	83	-

- No information, + Present but quantitative data not known, ? Disease suspected

2- AU-IBAR: The number of outbreaks reported to AU-IBAR is included in the Pan African Animal Resources Year Book. (**http://www.au-ibar.org/pan-african-animal-resources-yearbook?showall=&limitstart**=) and can be seen for the countries of interest in Table 3 below.

Table 3: Number of AAT outbreaks reported to the AU-IBAR from 2005 to 2015 (numbers given only for the target countries). Source: AU-IBAR Year Books.

Country	2005*	2006**	2007	2008	2009	2010	2011	2012	2013	2014	2015
West Africa											
Burkina Faso											
Ivory Coast							4			5	
Mali											
Senegal					1						
East Africa											
Ethiopia			5	7	12 cases	1	2				
Kenya		1	578	101	228 cases	419 cases	224	144	9	11	

Rwanda											
Tanzania		149	200	1215 cases	301 cases	392 cases	21	10	17	17	
Uganda		8	1	9	11	30	130	10	2	1	
Southern Africa											
Madagascar											
Malawi		1	1			1		1			
Mozambique		5	6	10	3	6	3		1		
South Africa		14		10	6	7	5	9	6	7	
Zambia			28	2	18	16	39	16	66	62	

*AU-IBAR didn't start yet producing data for AAT

Prevalence data by country

AFRICA

Burkina Faso

Year	*Area*	*Species of animal*	*No. of samples tested*	*% positive*	*Reference*
2009	southwestern Burkina Faso	crossbred cattle (Baoule-zebu peul)	363 followed over 2 years	Beginning of survey 7.5% based on PCV T. vivax 66.3% T. congolense 23.8%	Guiguigbaza-Kossigan Dayo et al. 2010

Ethiopia

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Amhara region, Northwest Ethiopia	Cattle	384	2.10%, only Tv found	Ayana et al. 2012
2007-2008	Eastern Wollega, Ethiopia	Cattle	424	15%	Tekle, 2012

Ivory Coast

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Northern Livestock Area		363	overall prevalence of 22.31% (PCR)	Kouadio et al; 2014

Kenya

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2010	Suba and Teso districts in Western	cattle	44 Teso & 59 Suba	41% Suba & 29% Teso	Thumbi et al. 2010

Madagascar

Never reported

Malawi

No prevalence study data could be found

Mali

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2009	Kadiolo Circle	Zebu, N'Dama and Zebu N'Dama cross	473	30.8% overall; 89%Tc, 9.5% Tv	Bocoum Z et al., 2012
2014	cercles de Kadiolo et Sikasso		1208	1.2%	Bass et al ; 2014

Mozambique

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2002*	Central	cattle	16895		Specht, 2008

*In smallholder cattle *T. congolense* was the predominant species at 41.53 %, followed by *T. vivax* at 31.84 % and *T. brucei* at 18.16 %; Infections with *T. vivax + T. congolense* accounted for 2.98 %, *T. vivax + T. brucei* for 2.32 %, *T. congolense + T. brucei* for 2.98 % and, with all three species, for 0.19 % of the infections. In commercial cattle *T. vivax* was the predominant species at 42.25 %, followed by *T. congolense* at 37.45 % and *T. brucei* at 15.68 %. Mixed infections accounted for 4.61 % of all infections.

Rwanda

No recent data could be found

Senegal

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2010	Western Senegal	cattle	1332	Overall 2.4%	Seck et al., 2010

Tanzania

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Northern Tanzania	indigenous Tanzania short horn zebu cattle	239	5%	Swai & Kaaya, 2012

Uganda

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Mulanda, Tororo District	Zebu cattle	300	5%	Nabulime et al, 2014
2014	Kitgum istrict	Zebu cattle	112	16.9%	Komakech R, 2014

Zambia

Year	Area	Species of animal	No. of samples tested	% positive	Reference
1988	South-West	Cattle	3,346	10.22%	Corten et al, 1988
2008-2010	North-Eastern	cattle	243	7.5% by PCR; 18.6% by PFR-LAMP, 6.1% microscopy	Laohasinnarong et al., 2015

Economic and Social Impacts at Global and Regional Levels, and in Selected Countries

In sub-Saharan Africa (SSA), -AAT- is one of the most important animal diseases - with more than 80 million cattle exposed to infective tsetse fly bites (*T. congolense, T. brucei brucei)* or infective tsetse fly and biting fly bites *(T. vivax)* [9]. It is estimated to cause annual losses that run into billions of dollars. AAT currently causes direct annual losses of some US$ 1.5 billion and, overall, has the effect of limiting Africa's agricultural income to some US$ 4.5 billion a year below its potential level [5].

African animal trypanosomiasis is indeed considered one of the root causes of hunger and poverty in most SSA countries where it represents a serious impediment to sustainable agricultural rural development. About 80% of land in SSA is tilled by hand due to the high risk of AAT that threatens the survival and use of draught animals. Trypanosomiasis is generally recognised as a very serious disease which may be fatal if left untreated. This is particularly true in susceptible animals, such as zebu cattle [10], but also trypano-tolerant animals, like N'Dama cattle, which may suffer from the pathological stress caused by trypanosomiasis, as assessed by anaemia development and reduced growth [1][10][18]. The FAO estimates that every year more than three million cattle die of trypanosomiasis [6]; in addition there are significant indirect losses to the livestock sector due to abortion, infertility, weight losses, reduced draught power, reduced milk production [12], all of which impact people's livelihoods and animal welfare. The fight against the disease is either managed by the control of the vector or of the parasite or a combination of both [12]. However, in poor rural communities, which are mostly affected by the disease, control is mainly relying on the use of trypanocidal drugs, irrespective of their quality [17].

Disease Prevention and Control Methods

Treatment (Control)

Methods for the control of the trypanosomiases has changed little in the last hundred years and still rely on four pillars of basic management: (i)the control of the vector, (ii) the correct diagnosis of the disease, (iii) the use of trypanocidal and prophylactic drugs and (iv) the use of trypanotolerant livestock. There is still no vaccine or immunisation method to date for AAT [5]. Integrated strategies, combining these different elements, but associated with very good animal husbandry are critical for successful and sustainable control and should be encouraged and implemented [23].

Vector control

Several approaches to fly control and eradication have been used with varying degrees of success.

Game elimination: this method which consisted in large-scale hunting of wild hosts of tsetse took place in Zimbabwe between 1930s and 1960, when it was abandoned [2]

The next methods focused on the fly.

Bush clearing: this consisted in the application of residual insecticides to tsetse resting sites by ground-based spraying teams. Extensively used in early tsetse fly eradication campaigns, has been locally useful because it eliminates the breeding places of the tsetse. But, to be completely effective, bush clearing requires ecologically unacceptable destruction of vast areas of brush and forest. It is still a useful procedure when used locally in conjunction with other control methods.

Since the relative success of these different approaches, which worked when accompanied by strict support systems, more other approaches have been employed in different regions and different times. These have included Trapping, aerial and ground spraying of insecticides, the use of dips or the application of pour-on formulations of insecticides to animals and the use of sterile male techniques, generally known as Sterile Insect technique or SIT.

Ground and aerial spraying with insecticides and the use of synthetic pyrethroids on cattle have lowered fly densities in some areas, but widespread use would require considerable international cooperation and expense. Widespread application of insecticide has the tremendous disadvantage of also eradicating many other arthropods, several of which are desirable. The recent introduction of odour-baited targets impregnated with insecticides is proving promising as a means of reducing the tsetse fly [7].

SIT: Inspired from the success of the sterile male technique on screwworm eradication in the United States, the SIT has been a big focus since the 1980s for Tsetse and Trypanosoma control and eradication. SIT is a genetic population suppression approach and involves sustained, systematic releases of irradiated sterile male insects among the wild population. The insects to be released are mass reared in large-scale insectaries. Males are sterilized by irradiation and then taken to the selected area and released by air. Early problems with breeding of the male flies have been overcome, and field trials have been done in both east and west Africa to determine the effectiveness of this approach in vector control. In limited trials, such as in the Unguja Island of Zanzibar, Tanzania [19] this procedure has succeeded in eliminating one type of Glossina, and in others reduced fly populations.

Chemotherapy

The use of trypanocidal drugs is currently the main method for controlling trypanosomiasis in all the countries where this disease occurs. Three compounds belonging to two chemical classes are widely available to treat trypanosomosis: diminazene diaceturate (belonging to the class of aromatic diamidines); and, isometamidium chloride hydrochloride and homidium (chloride and bromide salts) which belong to the phenanthridinium class of trypanocidal agents [14]

It is estimated that every year 25 to 30 million doses of curative and prophylactic anti trypanosomiasis drugs are administrated in Africa [14]. Ideally, their application should be under the control of qualified veterinary authorities but in fact this is rarely the case and most trypanocidal drugs are used directly by the livestock owners themselves, usually in the absence of definitive diagnosis of the disease. This situation has certainly promoted the invasion of the market with fake, non-effective trypanocidal drugs [17]. In addition there is evidence for the appearance of trypanosome strains that are resistant to these drugs.

Trypanotolerance

It has long been recognized that certain breeds of African cattle are considerably more resistant to African trypanosomiasis that others. This is especially true of the West African short-horned cattle (Muturu, Baoule, Laguna, Samba, and Dahomey) and the N'Dama, which is also of West Africa. Susceptibility studies have shown the N'Dama to be the most resistant breed followed by the smaller West African short-horned cattle, but the large and more recently introduced Zebu is the most susceptible [5][10]. Studies have revealed that a key element

of the resistance of this breed to trypanosome infection is its high ability to control the level of the parasitaemia and the anaemia [21], as illustrated in figure 7 below.

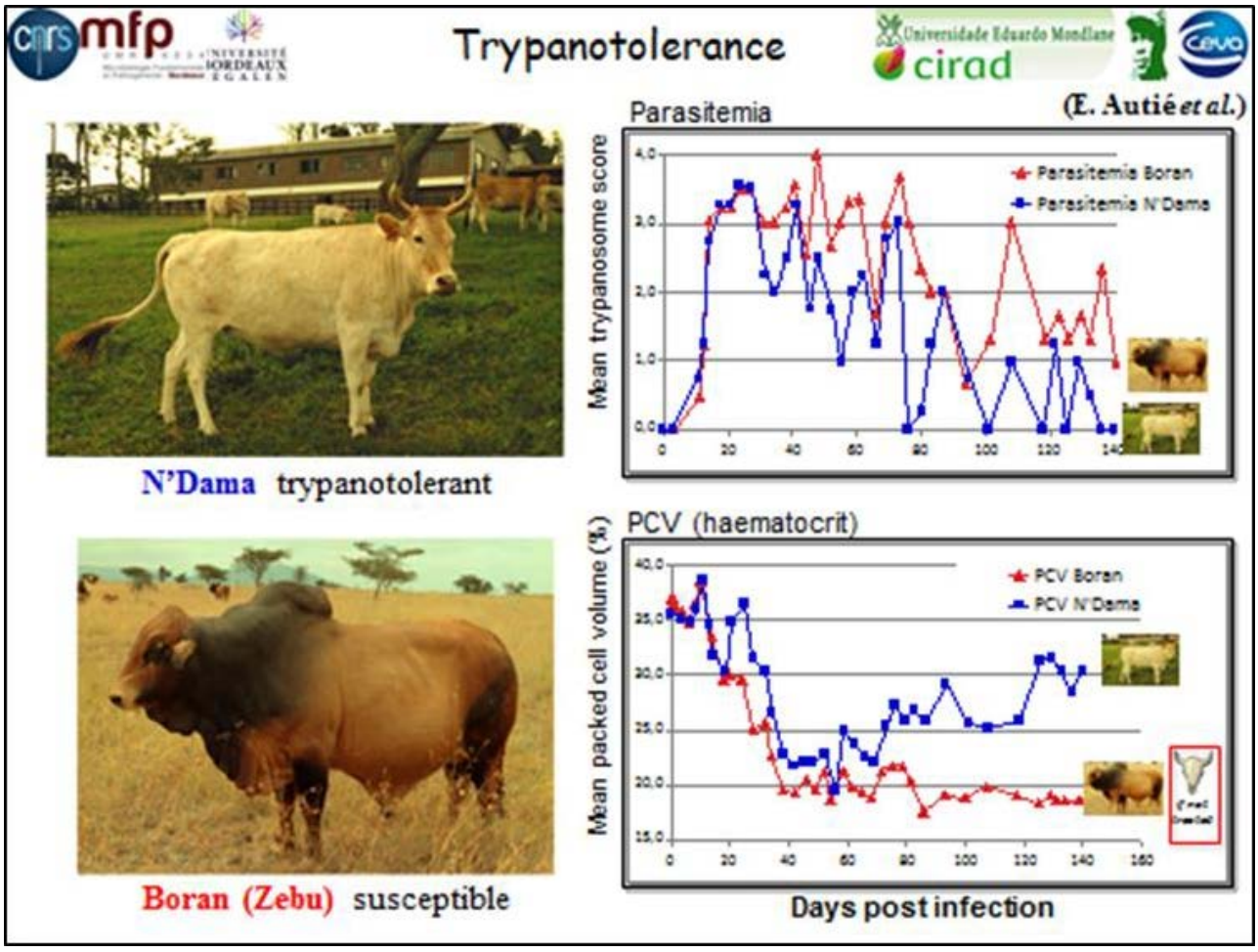


Figure 7: Evaluation of parasitemia and haematocrit between treapanotolerant cattle (NDama) and susceptible cattle (Boran); Source: adapted by Prof. T Baltz from Authié et al. [21]

Disease situation and government policies by country

Trypanosomosis is not a notifiable disease, and there is no vaccine, so it was not included in the questionnaires sent to the veterinary services of the countries of interest.

However, there are countries where control campaigns have been implemented, for example in Uganda, where the SOS Uganda program.

The Stamp Out Sleeping sickness (SOS) campaign is a public private partnership launched in Kampala, Uganda in October 2006. This partnership was formed in response to an emergency situation arising in a number of districts in Northern Uganda where the two strains of Human African Trypanosomiasis (HAT) – also known as "sleeping sickness"- threaten to converge. This could have a catastrophic effect for the already stretched local health services. Sleeping sickness threatens more than 66 million people in sub-Saharan Africa, whereof ten million in Uganda, killing more than 100 people a day.

For more details: **http://www.stampoutsleepingsickness.com/about-sos-.aspx**

http://www.ceva-africa.com/en/Responsibility/Program-supports/SOS-Uganda

AU-PATTEC, the African Union - Pan African Tsetse and Trypanosomiasis Eradication Campaign, was established following the adoption of Decision AHG/Dec. 156 (XXXVI) by the African Heads of States and Government during the OAU Summit held in Lome, Togo in July 2000, urging Member States to embark on a Pan African Tsetse and Trypanosomiasis Eradication Campaign. The PATTEC Coordination office was established in 2002 and was assigned the task of helping to initiate and coordinate the activities of the tsetse and Trypanosomiasis eradication campaign, within the framework of implementing the decision of the African Heads of State and Governments. The roles of PATTEC are:

- Identification of Target Areas
- Selection and Prioritization of Intervention Areas
- Project Initiation
- Project Support
- Harmonization of Different Programs
- Project Monitoring and Evaluation

The current PATTEC coordinator Dr Hassane H. Mahamat, has reactivated the organisation and taken a very proactive attitude. There are frequent meetings and activities, where the countries can provide updates on progress, and regional activities (for example the Congo Basin or Sudan) can be promoted.

For more details: **http://pattec.au.int/home**

Vaccines available

There is no vaccine available.

Characteristics of Ideal Vaccine Candidates for Smallholders

Although no vaccine is available to date, table 4 provides TPP that were developed in the context of GALVmed Trypanososmosis vaccine. This TPP was reviewed by panels of disease experts and has been published in GALVmed website: **http://www.galvmed.org/en/news/trypanosomosis/**

Table 4: Target Product Profile (TPP) Trypanosomosis vaccine – Proposal:

Attribute	Minimum	Ideal
1. Antigen	Immunogen with *T. congolense* &/or *T. vivax* antigens.	Immunogen with *T. congolense* & *T. vivax* antigens.
2. Indication for use	For active immunisation of cattle against *T. congolense* &/or *T. vivax*.	For active immunisation of cattle, sheep, goats & camels against *T. congolense* & *T.vivax*.
3. Target species	Cattle.	Cattle, sheep, goats, equines & camels.
4. Recommended Dose	≤5 ml (cattle).	Same dose for cattle and sheep: 2ml.
5. Pharmaceutical form	Reconstituted injectable solution/ suspension.	Ready to use solution/ suspension.
6. Route of administration	Subcutaneous or intramuscular.	Subcutaneous and intramuscular.
7. Regimen - primary vaccination course	Maximum of two doses given 2- 6 weeks apart.	Single dose.
8. Regimen - booster	6 monthly booster.	Annual dose.

9. Epidemiological relevance	Protection against *T. congolense* &/or *T. vivax* in affected regions.	Protection against T. congolense & T. vivax in affected regions.
10. Recommended age at first vaccination	When other vaccines are applied (normally 3-4 months of age).	From 1-2 months of age (as early as possible).
11. Onset of immunity	2-3 weeks following primary vaccination.	One week following primary vaccination.
12. Duration of immunity	Six months following first booster vaccination.	Life time immunity.
13. Expected efficacy	To prevent disease in > 70% of vaccinated animals [For registration studies: prevention of clinical disease (no proportional decrease in PCV greater than 20%*).]	To prevent infection and transmission in 100% of the animals. [For registration studies: absence of parasitaemia and clinical signs, and sustained normal haematocrit].
14. Expected safety	Mild and transient injection site reactions and pyrexia lasting less than 14 days. Transient milk reduction	No injection site reactions and no pyrexia nor milk reduction.
15. Withdrawal period	1-2 weeks at point of injection for meat.	Nil for milk and meat.
16. Special requirements for animals	Vaccinate only clinically healthy animals.	Vaccinate all animals.
17. Special requirements for persons	No severe reaction after accidental self-injection.	No reaction on self-injection.
18. Package size	10 and/or 50 doses.	<10, 50, 50, 100, 250 doses.
19. Price to end user	≤$5/dose	$1-2.00/dose to end user.
20. Storage requirements	Stable at 2-8°C for 24 months.	Stable at 30°C for 24 months.
21. Shelf-life as packaged for sale	18 months.	36 months.

22. Shelf-life after first opening (in-use stability)	1 hour.	24 hours or greater.
23. In-use preservative for inactivated vaccines	Any approved preservative.	No preservative required.

References

[1] Agyemang, K. Trypanotolerant livestock in the context of trypanosomiasis intervention strategies. PAAT Technical and Scientific Series No.1, FAO Rome, 66 pp. http://www.fao.org/docrep/007/y5832e/y5832e00.htm

[2] Connor RJ & Van den Bossche P 2004. African animal Trypanosomoses. In: COETZER, J.A.W. & TUSTN R.C. (eds). Infectious diseases of livestock (2nd edition). Cape Town: Oxford University Press: 251-295.

[3] Desquesnes M : Livestock Trypanosomoses and their Vectors in Latin America ; OIE (World organisation for animal health), 2004 http://www.oie.int/doc/ged/D9818.PDF

[4] d'leteren G.D.M, E. Authié , N. Wissocq & M. Murray: Trypanotolerance, an option for sustainable livestock production in areas at risk from trypanosomosis Rev. sci. tech. Off. int. Epiz., 1998,17 (1), 154-175; http://www.oie.int/doc/ged/D9189.PDF

[5] FAO Animal Production and Health Divison. PAAT - The Disease;. Available at: www.fao.org/Ag/againfo/programmes/en/paat/disease.html . Accessed on 01 Feb 2016

[6] Hursey, B.S., Slingenbergh, J. (1995). The tsetse fly and its effects on agriculture in sub-Saharan Africa. World Anim. Rev., **84/85**, 67-73.

[7] Kuzoe F.A.S & Schofield C.J.(2004): Strategic Review of Traps and Targets for Tsetse and African Trypanosomiasis Control; UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR; http://www.who.int/tdr/publications/documents/tsetse_traps.pdf

[8] Magez S, Caljon G, Tran T, Stijlemans B, Radwanska M (2010) Current status of vaccination against African trypanosomiasis. Parasitology 137: 2017-2027 https://www.researchgate.net/publication/44572412_Current_status_of_vaccination_against_African_trypanosomiasis

[9] Mattioli, R.C., Feldmann, U., Hendrickx, G., Wint, W., Jannin, J., Slingenbergh, J. (2004) - Tsetse and trypanosomiasis intervention policies supporting sustainable animal-agricultural development.; Food, Agriculture & Environment, **2**, 310-314.

[10] Mattioli, R.C., Jaitner, J., Clifford, D.J., Pandey, V.S., Verhulst, A. (1998). Trypanosome infections and tick infestations: susceptibility in N'Dama, Gobra zebu and Gobra x N'Dama crossbred cattle exposed to natural challenge and maintained under high and low surveillance of trypanosome infections. Acta Trop., **71**, 57-71.

[11] OIE (2013): Tsetse-transmitted Trypanosomosis disease card; **http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/TRYPANO_TSETSE.pdf**

[12] Shaw, A.P.M. (2009). Assessing the economics of animal trypanosomosis in Africa—history and current perspectives. Onderstepoort Journal of Veterinary Research, 76:27–32 (2009 **www.ojvr.org/index.php/ojvr/article/download/57/51**

[13] Spickler, Anna Rovid. "African Animal Trypanosomiasis Fact sheet" Sept 2009" At **http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php**

[14] Sutcliffe O.B., Skellern G.G., F. Araya, A. Cannavan , Sasanya JJ, Dungu B., van Gool F., S. Münstermann & Mattioli R.C: Animal trypanosomosis: making quality control of trypanocidal drugs possible; Rev. sci. tech. Off. int. Epiz., 2014, 33 (3), 813-830; **http://www.oie.int/fileadmin/Home/eng/Publications_%26_Documentation/docs/pdf/revue_plurithematique/2014/12092014-00040-EN-Sutcliffe.pdf**

[15] Tabel H, Wei G, Bull HJ (2013) Immunosuppression: Cause for Failures of Vaccines against African Trypanosomiases. PLoS Negl Trop Dis 7(3): e2090. doi:10.1371/journal.pntd.0002090

[16] Tabel H, Wei G, Bull HJ: Immunosuppression, induced upon intradermal infections, causes failures of vaccines against African trypanosomiases **http://www.usask.ca/wcvm/departments/microbiology/African%20trypanosomiasis%20vaccine%20II%2015-9-2012.pdf**

[17] Teko-Agbo A, Messomo Ndjana F, Walbadet L, Akoda K., Niang EL & Abiola FA: Quality of veterinary medicinal products in circulation in Cameron and Senegal; OIE Conference on Veterinary Medicinal Products in Africa, Dakar, 25-27 March 2008; **http://web.oie.int/eng/VETMED08/pdf_manuscrits/pdf_anglais/TEKO_fr_2603_Session2_Manuscript.pdf**

[18] Trail, J.C.M., Wissocq, N., d'Ieteren, G.D.M., Kakiese, O., Murray, M. (1994). Quantitative phenotyping of N'Dama cattle for aspects of trypanotolerance under field tsetse challenge. Vet. Parasitol., **55**, 185-195.

[19] VREYSEN M.J.B. Principles of area-wide integrated tsetse fly control using the sterile insect technique; Med. Trop.2001 ; 61 : 397-411

[20] World Organization for Animal Health: OIE Terrestrial Manual. Manual of Diagnostic tests and vaccines for terrestrial animals 2015. Accessed on line. **http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/**

[21] AUTHIÉ, E., DUVALLET, G., ROBERTSON, C. and WILLIAMS, D. J. L. (1993), Antibody responses to a 33 kDa cysteine protease of Trypanosoma congolense: relationship to 'trypanotolerance' in cattle. Parasite Immunology, 15: 465–474. doi: 10.1111/j.1365-3024.1993.tb00632.x **http://onlinelibrary.wiley.com/doi/10.1111/j.1365-3024.1993.tb00632.x/abstract;jsessionid=00CC3D707D22E92D1A0B08523D37F8AC.f01t01**

[22] Viljoen G J and Luckins AG (2012): The role of nuclear technologies in the diagnosis and control of livestock diseases—a review; Trop Anim Health Prod. 2012 Oct; 44(7): 1341–1366; **http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3433664/**

[23] Bouyer J, Bouyer F, Donadeu M, Rowan T, Napier G. Community- and farmer-based management of animal African trypanosomosis in cattle. Trends Parasitol. 2013;29 (11):519–22.

ANNEX 1: Additional data on disease presence and incidence

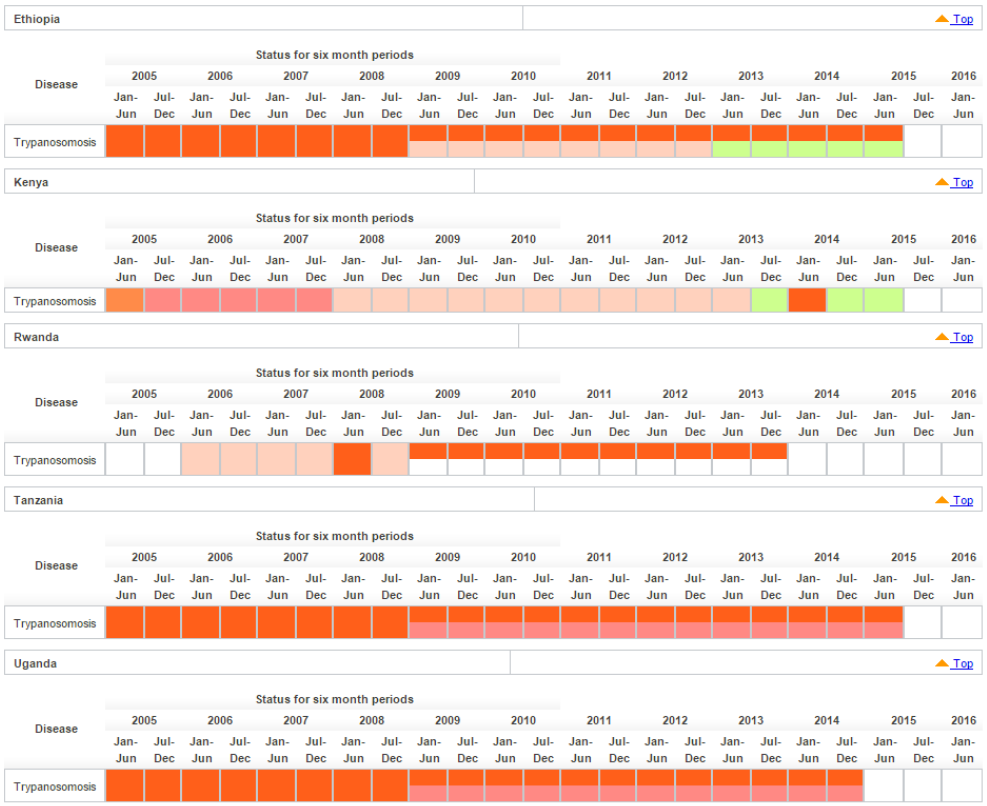
Reports to OIE on Trypanosomosis. Please note that the OIE only mentions Trypanosomosis, without specifying the type.

Key to colours

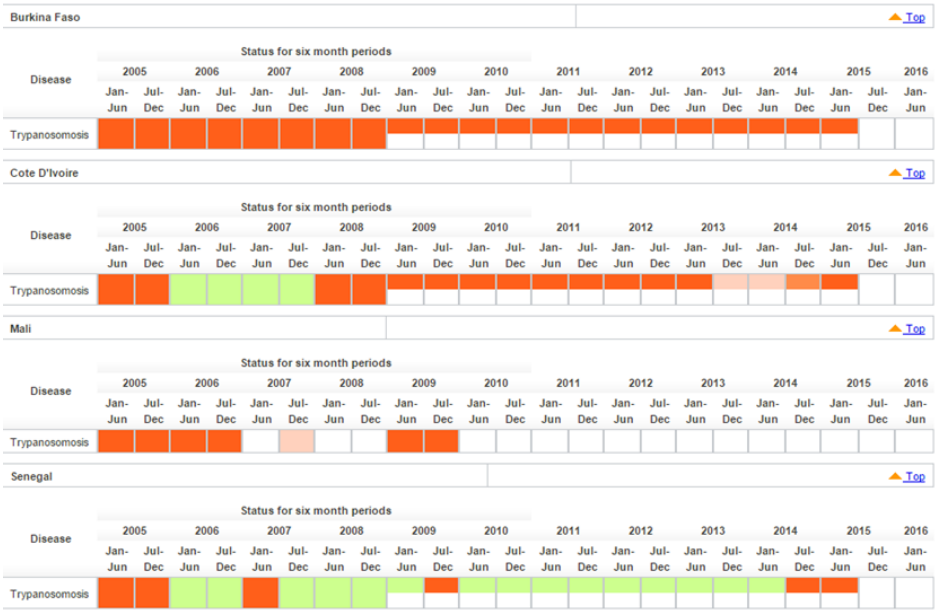
- There is no information available on this disease
- Never reported
- Disease absent
- Disease suspected but not confirmed
- Infection/infestation
- Disease present
- Disease limited to one or more zones
- Infection/infestation limited to one or more zones
- Disease suspected but not confirmed and limited to one or more zones

When different animal health statuses between domestic and wild animal population are provided, the box is split in two: the upper part for domestic animals, and the lower part for wild animals.

Trypanosomosis in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda



Trypanosomosis in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal



Trypanosomosis in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia